

REMARKS

Applicants acknowledge receipt of the Office Action, dated March 2, 2004. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim 9 is cancelled without prejudice to subsequent reinstatement of deleted subject matter, for example, in one or more divisional applications. Claims 1-8, 10, 12-19, 23, 25, and 28 are currently being amended. No claims are being added. This amendment changes and/or deletes claims in this application. A detailed listing is presented, with an appropriate defined status identifier, of all claims that are or were in the application, irrespective of whether the claim(s) remain under examination.

After amending the claims as set forth above, claims 1-8 and 10-28 will be pending. Claims 21, 22, and 26 are withdrawn from further consideration. Claims 1-8, 10-20, 23-25, 27, and 28 are presented for consideration by the Examiner.

Applicants have amended claims 1, 13, 15, and 16 by replacing the term "teratocarcinoma" with "carcinoma," for the sake of clarity. The phrases "embryonal teratocarcinoma cell" and "embryonal teratocarcinoma nucleus" in these claims are revised now to read "embryonal carcinoma cell" and "embryonal carcinoma nucleus," respectively. This amendment is supported by the specification, where the applicants describe the invention with respect to embryonal carcinoma ("EC") cells (*see, e.g.*, page 9, lines 12-28; page 10, lines 4-5; page 10, lines 11-14; page 10, lines 21-26; page 11, lines 12-15; page 13, lines 5-13; page 13, lines 17-20; page 14, lines 1-17; page 14, lines 24-30; page 15, lines 8-9; Tables 1 and 2; Figures 1-4; and the experimental section from page 18, line 21 to page 35, line 5).

In addition, Applicants have amended claim 1, by replacing the indefinite article "a" with "an" before "embryonal carcinoma cell." This amendment is made to correct the grammar.

Finally, a clarifying amendment is made to claims 18 and 28 to modify the phrase "cytoplasm/somatic cell fusion" to "cytoplasm or somatic cell fusion." Furthermore, to provide

an antecedent for "said cytoplasm," claim 18 is made dependent on claim 17. Basis for this amendment is found in the original claims.

OBJECTIONS

The Examiner objected to claims 2-10 for reciting "a cell according to claim ..." rather than "the cell," and to claim 28 for reciting "a method according to claim 17 ..." rather than "the method." Applicants have amended claims 2-8, 10, and 28 to comply with this formality. Additionally, applicants have amended claims 12, 14, 17, 18, 19, and 25, even though these claims have not been objected to by the Examiner on the same ground.

The Examiner further objected to claim 9 for the misspelling of the term "pluripotential." Claim 9 is cancelled rendering the objection moot.

Finally, the Examiner objected to claim 10 for the misspelling of the term "characterized." The typographical error relating to the word "characterized" in claim 10 has been corrected in the enclosed amended claims. Furthermore, although not objected to by the Examiner, the word "characterised" has been replaced by "characterized" in claims 2-8, 12, 14, 17-19, 25, and 28.

REJECTIONS

35 U.S.C. § 101 – Statutory Subject Matter

The Examiner has rejected claims 1-10 and 23 under 35 U.S.C. § 101 because they are allegedly not directed to statutory subject matter. Specifically, the Examiner asserts that the claims as recited "encompass any somatic cell that has been differentiated from an embryonic teratoma, or a naturally occurring teratoma." In response, Applicants have added the term "isolated" to claim 1, so that it recites "An isolated cell ...," and to claim 23, so that it recites "At least one isolated tissue type or isolated organ ..." The Examiner has indicated that this addition will obviate the objection.

35 U.S.C. § 112, ¶ 1 – Enablement

With respect to the enablement rejection of claims 1-20, 23-25, 27, and 28 under 35 U.S.C. § 112, first paragraph, the Examiner asserts that Applicants have not shown that the

claimed methodology produces cells that possess at least one pluripotent characteristic, which includes the ability to differentiate into at least two selected tissue types. Further, the Examiner asserts that “it is known in the art that the expression of Oct4 is not necessarily an indicator of pluripotency.”

In response, Applicants submit that it is well-known that *Oct4* expression is indicative of pluripotency. See, e.g., Brehm *et al.*, APMIS. 106(1):114-24 (1998), discussed in the specification at page 28, lines 9-24. In the same vein, Applicants provide a recent article by Flaszka *et al.*, *Cloning & Stem Cells* 5: 339-54 (2003), which validates their teaching that the disclosed method of reprogramming forms a cell possessing at least one pluripotential characteristic, as evidenced by the expression of *Oct4*. Thus, Flaszka *et al.* have shown that PEG-mediated fusion of murine EC cell line P19 with a human T-lymphoma cell line (CEM-GFP) resulted in reprogramming of the human somatic cell to exhibit pluripotential characteristics, such as *Oct4* and *Sox-2* expression.

That those working in the field accept *Oct4* expression as evidence of pluripotency vindicates Applicants’ own invocation of *Oct4* expression in the present context. Applicants further submit that the finding of Monk & Holding (2001), that *Oct4* is expressed in human tumors, does not denigrate *Oct4* as a pluripotency marker, contrary to the Examiner’s speculation on this subject.

It is widely considered that, during the development of certain malignancies, the malign cells re-establish their pluripotency. Certainly, it has long been observed that malignant cells express embryonic markers. Indeed, Monk and Holding themselves state that “cancer cells are also immortal, undifferentiated and invasive. Therefore, it might be expected that cancer cells will express genes in common with these very early embryonic cells, especially genes specifically associated with deprogramming and return to the undifferentiated and proliferative stem cell state” (page 8085, second column, first full paragraph).

Embryonic stem (“ES”), embryonic germ (“EG”), and EC cells are authentic pluripotent cells *and* are capable of tumor formation (see present application, page 10, lines

11 to 13). Therefore, the Examiner is not at liberty to dismiss the significance of genes, such as *Oct4*, that are expressed in a pluripotent cell, merely because those genes also are expressed in a tumor cell. The hallmarks of pluripotency are established anew in a subset of tumor cells. Therefore, the pluripotency of the cells in the specific examples of the present application cannot justifiably be denied by saying that the *Oct4* marker is present in certain tumor cells. Applicants submit that pluripotency has been established in the cells made by the claimed methods using the *Oct4* marker.

The Examiner has noted in the paragraph flanking pages 7 to 8 of the Office Action that the human EC cell line, TERA1, appeared to be unable to reprogram mouse thymocytes, as shown by the lack of expression of mouse *Oct4*. Applicants submit that, as one of ordinary skill in the art would appreciate, the formation of hybrids between two cells of the same species occurs at a frequency as low as 10^{-4} to 10^{-5} , and that formation of hybrids between two cells of different species may occur at an even lower frequency. It is not unexpected that formation of hybrids between a particular pair of cell types may occur at a higher or lower frequency than another pair of cell types. Indeed, cell-cell fusion is a genetically controlled event and may be subject to the same variations as any other Mendelian trait in the genome. Thus, 2102Ep cytoplasm may appear to reprogram partner thymocytes more readily than TERA1 cytoplasm due to a relative inefficiency of TERA1 cells in forming fusions.

Furthermore, as the majority of cells in fusion experiments remain unfused, one of ordinary skill in the art would appreciate that the assay used to detect reprogramming should be robust in order to compensate for the paucity of fused, and potentially reprogrammed and pluripotent, cells. The amplification of expressed sequences using polymerase chain reaction ("PCR") has a finite capacity to detect rare events in gene expression. Thus, the detection of *Oct4* expression in fusions between 2102Ep cells and murine thymocytes may have been just above a detectable limit (*i.e.*, extrapolating from a theoretical frequency of fusion, a limit of detecting 1 fused and reprogrammed cell per 10,000 unfused cells). If TERA1 cells yielded fewer fusion events, then the skilled person would appreciate that it is possible that potential reprogramming events might not have been detectable using PCR technology. Other means

of measuring reprogramming and pluripotency might show that TERA1 was equally capable of reprogramming thymocytes in fusions.

In the teachings of Flaszka *et al.*, *supra*, Applicants also have more recent evidence that the disclosed method of reprogramming to form a cell possessing at least one pluripotential characteristic is not specific for 2102Ep cells. As noted, Flaszka and co-workers demonstrated that PEG-mediated fusion of murine EC line P19 to human T-lymphoma line CEM-GFP resulted in reprogramming of the human somatic cell to exhibit pluripotential characteristics such as *Oct4* and *Sox-2*. Accordingly, the murine EC cell line P19 is a further example of an EC cell competent to cause reprogramming of the nucleus of a differentiated somatic cell to exhibit an art-recognized pluripotential characteristic.

In the paragraph flanking pages 9 and 10 of the action, the Examiner asserts that some of the claims are directed to methods of generating a nuclear transfer ("NT") unit, where the nuclear transfer unit is further cultured under conditions to proliferate the NT unit, and that these claims are not enabled as they do not provide steps showing activation of the NT unit which, according to Dinnyès *et al.* (2002), must take place. Applicants submit, however, that the present application does not concern an NT unit as referred to by Dinnyès *et al.* (2002). Activation is only required where, and inasmuch as, it mimics the act of fertilization brought about by the sperm contacting the egg. In the case of NT, no such sperm exists and thus the activation must be brought about as mentioned by Dinnyès *et al.* (2002). Activation to achieve pluripotency in EC, ES, or EG cells has already occurred. For somatic cell reprogramming by an EC cell, *i.e.*, via the means demonstrated or described in the present application, no like activation is required because the new pluripotent cells are not being established through an oocyte. Therefore, the claims of the present application do not need to recite steps of activation as suggested by the Examiner.

In the paragraph bridging pages 11 and 12, the Examiner refers specifically to claim 5 which is directed to a pluripotential cell expressing *Oct4*. The Examiner states that the "specification fails to provide sufficient teachings or guidance to show that the NT [nuclear transfer] unit itself would express Oct-4, as the specification clearly teaches the growth and proliferation of the original nuclear transfer unit for 2 days prior to analysis for Oct-4

expression.” Applicants submit, first, that the concept of “NT unit” is not directly applicable to the present invention for reasons stated above and, second, that the cell claimed in claim 5 must have at least one pluripotential characteristic by dependency on claim 1. Therefore, a cell that possesses an “NT unit” (as referred to by the Examiner) but that does not have a pluripotential characteristic is not within the scope of the claims, and Applicants should not be required to show support, as suggested by the Examiner, for a cell that is not claimed.

35 U.S.C. § 112: Indefiniteness

The Examiner has rejected claims 1-20, 23-25, 27, and 28 as indefinite because they recite a cell which has “the ability” to differentiate into at least two selected tissue types. The Examiner asserts that this phrase is unclear because it describes a “latent property,” but that “the conditions for the latent property” are not clearly defined so “it is unclear if the latent property is ever obtained.”

The Examiner’s objection is not well-founded, however, because one of skill in the art readily would understand what is meant by “the ability to differentiate into at least two selected tissue types” in the context of pluripotential cells. Simply put, the quoted phrase means that the cells are capable of differentiation into at least two different tissue types, for example, upon stimulation by a differentiation factor (*see* specification, page 7, lines 14-29; and page 10, lines 28-30). Furthermore, the present application at page 30, line 25, to page 31, line 21, provides conditions which one of ordinary skill in the art might use to cause differentiation of the isolated cell recited in claim 1.

In this respect, Applicants refer the Examiner to Thomson US patent No. 5,843,780 (copy enclosed), granted from WO 96/22362, which is cited in the present application at page 3, lines 9 to 23, and which the Examiner invokes against the present application, as discussed below. On page 1, lines 21-25 of Thomson, stem cells are defined as pluripotent, meaning that the cells possess “the capability of developing into any organ or type.” Claim 1 of US Patent No. 5,843,780 recites a purified preparation of primate embryonic stem cells which, amongst other things, “maintains the potential [i.e. the ability] to differentiate into derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture.” No further

“conditions for the latent property,” as referred to by the Examiner, are recited in claim 1 of US Patent No. 5,843,780. Therefore, applicants submit that the Examiner is incorrect in her objection to the clarity of claim 1. Her objection furthermore appears to be inconsistent with USPTO practice.

Claim 1 is further objected to as being further unclear because it states that (at least part of) the cytoplasm of the cell is “derived from” an embryonal carcinoma cell. Claim 1 has therefore been amended to recite that at least part of the cytoplasm is “from an embryonal carcinoma cell,” *i.e.*, the term “derived” has been deleted. A basis for this amendment can be found for example at page 1, lines 4-7, page 5, lines 12-14, and page 10, lines 4-5, of the present application. It is submitted that amended claim 1 is clear to one of ordinary skill in the art in specifying that the cell of the invention in one aspect comprises at least part of the cytoplasm which is from an embryonal carcinoma cell.

Similarly, claim 1 and claim 16 have been amended for the sake of clarity to recite that the cell “contains a genome only from the differentiated somatic cell.” Therefore, it is now clear that the nucleus may contain factors such as transcription factors other than the genome, but that the genome component of the nucleus is from the differentiated somatic cell. Also, the question of how the genome might be “derived” from a somatic cell is rendered void. Therefore, it is submitted that claim 1 (and claims 2-8, 10-20, 23-25, 27, and 28, which are dependent thereon) and claim 16 are clear.

The Examiner has rejected claim 3 as indefinite because the cell has “the capacity” to proliferate but that it is “unclear if this property occurs or not.” Applicants refer the Examiner to the discussion above, regarding the term “ability” in claim 1, and they submit that a skilled person would appreciate that the claimed cell possesses the property to be able to proliferate in culture in an undifferentiated state. Whether this property is exhibited in a particular instance depends on whether the cell is maintained in conditions that allow the undifferentiated state to continue, or whether differentiation is induced (see page 29, line 8, to page 31, line 21 of the present invention); but the claimed cell is capable of either fate.

In this regard, Applicants again note claim 1 of US patent No. 5,843,780, derived from Thomson, which recites a purified preparation of primate embryonic stem cells that, amongst other things, “is capable of proliferation in an in vitro culture for over one year.” As stated on page 23, lines 26 to 33 of Thomson: “Immortal cells are capable of continuous indefinite replication in vitro. Continued proliferation for longer than one year of culture is a sufficient evidence for immortality, as primary cell cultures without this property fail to continuously divide for this length of time (Freshney, Culture of animal cells. New York: Wiley-Liss, 1994).” Therefore, Applicants submit that claim 3 is definite and clear.

The Examiner also has asserted that claim 5 is indefinite because the claim is said to recite that “the cell has ‘the capacity’ to proliferate [see lines 1-2 of the claim].” According to Applicants’ records, however, claim 5 recites a cell that expresses the marker *Oct4*, and does not mention the words “the capacity.” Applicants thus request clarification or withdrawal of the Examiner’s objection.

In response to the indefiniteness rejection of claim 9, Applicants note that they have cancelled claim 9 without prejudice to subsequent reinstatement of deleted subject matter in one or more divisional applications, therefore rendering the rejection moot.

35 U.S.C. § 102: Anticipation

The Thompson Reference

The Examiner rejected claims 1-12, 20, 23-25, and 27 as allegedly anticipated by Thompson (WO 96/22362). Thompson teaches the isolation and purification of primate ES cells capable of indefinite proliferation *in vitro* in an undifferentiated state. The Examiner has argued that Thomson teaches the claimed invention because “the teratomas as taught by Thomson have at least part of the cytoplasm derived from an embryonal teratocarcinoma cell, and a nucleus that contains a genome derived from a differentiated somatic cell” (*see* pages 15-16).

In response, Applicants note that claim 1 now recites an isolated cell with cytoplasm from an embryonal carcinoma cell and a nucleus with a genome from a differentiated somatic cell.

In addition, Applicants observe that, in the experiment where rhesus ES cells are injected into the hind leg muscles of SCID mice, Thomson discloses the production of tumors containing a variety of differentiated tissue types representing the three embryonic germ layers (*see* Thomson page 21-22). The tumors described in Thompson are not disclosed as containing EC cells as required by claim 1. As the Examiner may be aware, EC cells resemble early embryonic cells and are the stem cells that give rise to all the other cell types in germ cell tumors (“GCT”) except seminoma. While EC cells have been shown to share many features with ES cells, EC cells are a separate entity with distinguishable characteristics (for example, mutations that result in the malignant phenotype of EC cells). By comparison, ES cells used by Thomson are derived from the inner cell mass of a developing embryo and have no relation to the embryonal carcinoma cells of our invention. The Examiner’s statement that tumors “as taught by Thomson have at least part of the cytoplasm derived from an embryonal teratocarcinoma cell” (Office Action, page 16, first full sentence) is not correct because teratocarcinoma cells or EC cells were not demonstrated in Thomson’s example. Furthermore, none of the cells in the tumors described by Thomson involve cells that have been produced by combining the cytoplasm from an EC cell and the nucleus of a somatic differentiated cell.

Therefore, Thompson does not disclose an isolated cell comprising a single nucleus, where the cell possesses at least one pluripotential characteristic, which characteristic includes the ability to differentiate into at least two selected tissue types, where the cell comprises either (i) at least part of the cytoplasm from an embryonal carcinoma cell, or (ii) a cytoplasm from an embryonal carcinoma cell, and where the cell has its nucleus obtained from a differentiated somatic cell and contains a genome only from the differentiated somatic cell as recited in claim 1. In addition, it does not disclose a cell line or cell culture comprising such an isolated cell, an isolated tissue type or isolated organ comprising such an isolated cell, a therapeutic composition comprising such an isolated cell, or a kit comprising such an isolated cell. As such, Thompson does not disclose each and every claim limitation of claim 1 and therefore does not anticipate claim 1. Since claims 2-8, 10-12, 20, 23-25, and 27 depend on claim 1, for at least this reason, these claims are patentable over Thompson.

The Warejcka Reference

The Examiner rejected claims 1, 4, 6, 11, 20, 23-25, and 27 as allegedly anticipated by Warejcka *et al.* (1996). The Examiner states that these claims are anticipated by Warejcka, which teaches the isolation of “stem cells” from rat hearts. Specifically, the Examiner asserts that:

Warejcka teach the claimed invention because the cells only require the ability to differentiate into two selected cell types. Furthermore, the cells, as claimed merely require that the cytoplasm of the cells be ‘derived from’ an embryonal teratocarcinoma cell, and that the nucleus be ‘derived from’ a differentiated somatic cell. Thus, a cell, as described by Warejcka anticipates the claimed cells because one of skill in the art would not be able to tell the difference between cells that had cytoplasm derived from an embryonal teratocarcinoma cell, and cells of the art.

(Office Action, page 18, third paragraph).

In response, Applicants note that present claim 1 recites an “isolated cell,” with cytoplasm from an EC cell and a nucleus with a genome from a differentiated somatic cell. The Examiner’s comments with respect to the term “derived from” are rendered moot, therefore, as the cells taught by Warejcka clearly do not comprise cytoplasm from an embryonal carcinoma cell and a nucleus with a genome from a differentiated somatic cell.

Additionally, Warejcka teaches that the cells isolated from rat hearts were mesodermal stem cells (see Abstract, for example). Accordingly, the stem cells are limited to differentiation along a pathway that gives rise to mesodermal derivatives some of which are described in the publication. By the same token, the cells taught by Warejcka are not pluripotent and would not be expected to express *Oct4*, or any markers characteristic of pluripotent cells such as those described in the present application (for example SSEA-1, SSEA-3 and TRA-1-60). Furthermore, the cells taught by Warejcka would not be expected to give rise to derivatives of the other two germ layers, namely ectoderm and endoderm, whereas the cells of our invention would be.

Contrary to the Examiner's assertion, therefore, one skilled in the art would be able to distinguish the cells of Warejcka and the cells of the present invention. This is so because the cells of the present invention, but not those of Warejcka, express markers of pluripotency (such as SSEA-3, SSEA-4, TRA-1-60 and/or *Oct4*) and can give rise to differentiated products, including but not limited to those of the mesodermal lineage.

Accordingly, there is no disclosure in Warejcka that implicates Applicants' claimed invention. In particular, Warejcka does not disclose an isolated cell comprising a single nucleus, where the cell possesses at least one pluripotential characteristic, which characteristic includes the ability to differentiate into at least two selected tissue types, where the cell comprises either (i) at least part of the cytoplasm from an embryonal carcinoma cell, or (ii) a cytoplasm from an embryonal carcinoma cell, and where the cell has its nucleus obtained from a differentiated somatic cell and contains a genome only from the differentiated somatic cell as recited in claim 1. In addition, the reference does not disclose a cell line or cell culture comprising such an isolated cell, an isolated tissue type or isolated organ comprising such an isolated cell, a therapeutic composition comprising such an isolated cell, or a kit comprising such an isolated cell. For these reasons, Warejcka does not disclose each and every claim limitation of claim 1 and, hence, cannot anticipate claim 1 or its dependents, claims 4, 6, 11, 20, 23-25, and 27.

The Pera Reference

Finally, the Examiner rejected claims 1-12, 20, 23-25, and 27 as allegedly anticipated by Pera *et al.* (1989). Pera teaches the isolation and characterization of the human teratoma cell line, GCT27. The Examiner asserts on pages 19-20 of the Office Action that the disclosure of the GCT27 cell line in Pera anticipates the present invention. The Examiner bases her conclusion on the assertion that the disclosed cell line has "at least part of the cytoplasm derived from an embryonal teratoma cell, and because the nucleus of the cell need only be 'derived' from a differentiated somatic cell, such a cell could be a reprogrammed cell, which would be identical to that of the cells taught by Pera."

In response, Applicants note that the invention of claim 1 now recites an isolated cell with cytoplasm from an EC cell and a nucleus with a genome from a differentiated somatic cell. The Examiner's comments with respect to the term "derived from" are therefore rendered moot, as the cells taught by Pera clearly do not comprise cytoplasm from an embryonal carcinoma cell and a nucleus with a genome from a differentiated somatic cell.

Indeed, the cells taught by Pera are an EC cell line and, as with 2102Ep, TERA1, or P19 referred to in the description of the present invention, they could be used to produce the cells of the present invention. The EC cell taught by Pera, however, was not obtained by combining a cytoplasmic part of an EC cell and a nucleus of a differentiated somatic cell, but arose from a malignant transformation which produced the cell line GCT27. Cells from the GCT27 cell line are clearly distinguishable from cells of the present invention because tumors are created due to many mutations that accumulate during the development of malignancy and, while some of the mutations are commonly observed in certain tumors, the causes of these mutations are not well known for individual tumors. The nucleus of a tumorigenic EC cell of the kind taught by Pera cannot be used to anticipate a claim directed to the nucleus of a somatic cell because of the accumulated mutations. Furthermore, in the case of EC cells of the present invention, it is generally believed that tumors originate from germ cells in both their gonadal and extra-gonadal forms. By definition, germ cells are not somatic cells.

Accordingly, Pera does not disclose an isolated cell comprising a single nucleus, where the cell possesses at least one pluripotential characteristic, which characteristic includes the ability to differentiate into at least two selected tissue types, where the cell comprises either (i) at least part of the cytoplasm from an embryonal carcinoma cell, or (ii) a cytoplasm from an embryonal carcinoma cell, and where the cell has its nucleus obtained from a differentiated somatic cell and contains a genome only from the differentiated somatic cell as recited in claim 1. In addition, it does not disclose a cell line or cell culture comprising such an isolated cell, an isolated tissue type or isolated organ comprising such an isolated cell, a therapeutic composition comprising such an isolated cell, or a kit comprising such an isolated cell. As such, Pera does not disclose each and every claim limitation of claim 1 and

therefore does not anticipate claim 1. Since claims 2-8, 10-12, 20, 23-25, and 27 depend on claim 1, for at least this reason, these claims are patentable over Pera.

In summary, the present invention describes combining at least part of a cytoplasm (or cytoplast) of an EC cell and a nucleus obtained from a differentiated somatic cell, to generate a pluripotent cell that is not embryonic or fetal in origin, *i.e.*, that has not been "derived" or isolated from an embryo or fetus. The product of the process, an isolated cell as recited in claim 1, is not an ES cell (as taught by Thomson), or an adult stem cell (as taught by Warejcka), or an EC cell *per se* (as taught by Pera). Therefore, none of the cited prior art anticipates the presently claimed invention.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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